

SUPPLEMENTARY DATA

Supplementary Appendix 1. Inclusion/exclusion criteria for participants without type 1 diabetes

- a. < 35 or > 60 yrs.
- b. Non-English speaking
- c. HTN history or taking medications for HTN.
- d. Regular night shift.
- e. Insulin dependent diabetic.
- f. Any cardiac disease, insulin dependent diabetes, seizure disorder, unconscious > 30 mins, amnesia > 24hrs, more than 2 episodes of MTBI, any physical or psychological problem you deal with on a daily basis for 3+ months, chronic liver or kidney disease, treatment for cancer in the past 12 months, serious neuropsychiatric conditions, stroke, multiple sclerosis, brain tumor.
- g. Metal in body, refused for an MRI or refused themselves – claustrophobia.
- h. Current pregnancy.
- i. >30% overweight by Metropolitan Life Insurance table standards
- j. Medications – see below.

Medications – any cardiac medication on a routine basis – exclude and for certain categories on a regular basis: anti-anxiety**, narcotics*, antihistamines*, sleeping pills**, inhaled medications for asthma, COPD (chronic bronchitis, emphysema) – exclude - */** exceptions are made for those taking less than half of the time, but they must abstain for *= 24hrs and ** = 72 hrs.

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Supplementary Table 1. Ordinal logistic regression models showing the effects of diabetes-specific factors on the odds of cognitive impairment, controlling for years of education. Measures taken at time of cognitive assessment (2010-2013) unless otherwise noted. Odds ratios here should be interpreted proportionately as: the odds of any cognitive impairment (1+ vs. 0 tests impaired at 1.5+ SD compared to published norms); also 2+ vs. 0-1 tests impaired.

Model	1	2	3	4	5
	Odds Ratio (95% Confidence Limits)				
Years of education	0.79 (0.67, 0.93) <i>p</i> =0.004*	0.78 (0.66, 0.92) <i>p</i> =0.004*	0.78 (0.66, 0.92) <i>p</i> =0.003*	0.78 (0.66, 0.92) <i>p</i> =0.003*	0.78 (0.66, 0.93) <i>p</i> =0.006*
Average (1996-2013) HbA1c ≥ 7.5%	3.03 (1.31, 6.99) <i>p</i> =0.01*				
Prevalent proliferative retinopathy †		2.79 (1.23, 6.33) <i>p</i> =0.01*			
Prevalent distal symmetric polyneuropathy †			2.55 (1.13, 5.75) <i>p</i> =0.03*		
BMI (kg/m ²)				1.10 (1.01, 1.20) <i>p</i> =0.03*	
Ankle-brachial index ≥ 1.3 or non-compressible †					4.19 (1.38, 12.72) <i>p</i> =0.01*

* Statistically significant using Bonferroni corrected *p*<0.03

† assessed at EDC exam in years prior to cognitive testing; interval from 2004-2006 assessment to cognitive testing (2010-2013) added to model

Variables in Model:

Model 1: Years of education + 14-year average HbA1c ≥ 7.5%

Model 2: Years of education + prevalent proliferative retinopathy (assessed 2004-2006)

Model 3: Years of education + prevalent distal symmetric polyneuropathy (assessed 2004-2006)

Model 4: Years of education + BMI

Model 5: Years of education + ABI ≥ 1.3

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Supplementary Table 2. False discovery rate calculations (FDR=0.2) using the Benjamini-Hochberg correction method to determine statistical significance (“TRUE” vs “FALSE”) when comparing factors between participants with compare to participants without type 1 diabetes (main text, Table 1).

<i>i</i>	<i>p</i>	<i>q*</i>	<i>p < q*</i>	Factor
1	0.0000	0.0200	TRUE	Serum glucose
2	0.0000	0.0400	TRUE	DBP
3	0.0001	0.0600	TRUE	History of high blood pressure
4	0.0030	0.0800	TRUE	Education
5	0.0300	0.1000	TRUE	Physical activity
6	0.1100	0.1200	TRUE	BMI
7	0.1200	0.1400	FALSE	Apo E4 (24, 34, 44)
8	0.5100	0.1600	FALSE	Female
9	0.7200	0.1800	FALSE	Age
10	0.9100	0.2000	FALSE	SBP

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Supplementary Table 3. False discovery rate calculations (FDR=0.2) using the Benjamini-Hochberg correction method to determine statistical significance (“TRUE” vs “FALSE”) when comparing factors between participants with type 1 diabetes by cognitive impairment status (main text, Table 1).

<i>i</i>	<i>p</i>	<i>q*</i>	<i>p < q*</i>	Factor
1	0.0040	0.0095	TRUE	Education
2	0.0100	0.0190	TRUE	14-yr average A1c > 7.5%
3	0.0100	0.0286	TRUE	A1c > 7.5%
4	0.0300	0.0381	TRUE	Distal symmetric polyneuropathy *
5	0.0300	0.0476	TRUE	Proliferative retinopathy *
6	0.0500	0.0571	TRUE	BMI
7	0.0500	0.0667	TRUE	Average ABI > 1.3 †
8	0.0600	0.0762	TRUE	24-year A1c months
9	0.1500	0.0857	FALSE	Estimated glomerular filtration rate *
10	0.1500	0.0952	FALSE	Coronary artery disease *
11	0.1800	0.1048	FALSE	Physical activity *
12	0.2600	0.1143	FALSE	Age
13	0.2900	0.1238	FALSE	T1D duration
14	0.3700	0.1333	FALSE	Cardiac autonomic neuropathy *
15	0.3800	0.1429	FALSE	History of high blood pressure
16	0.4700	0.1524	FALSE	SBP
17	0.5000	0.1619	FALSE	DBP
18	0.6100	0.1714	FALSE	Age at T1D diagnosis
19	0.93	0.180952	FALSE	Serum glucose
20	0.96	0.190476	FALSE	Female
21	0.97	0.2	FALSE	Apo E4 (24, 34, 44)

All measures from time of cognitive testing unless otherwise specified

* measured in 2004-2006

† measured in 1990-1992

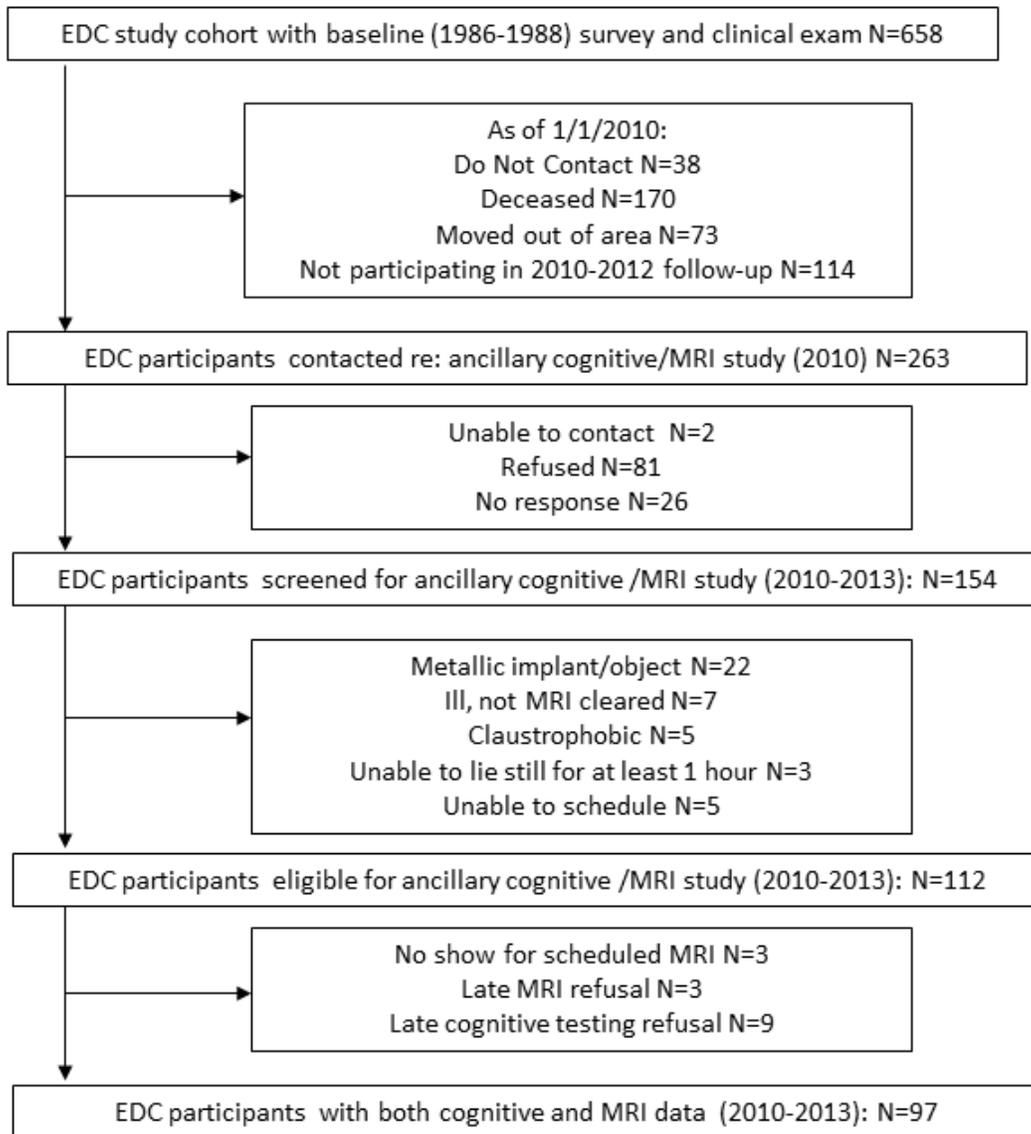
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Supplementary Table 4. False discovery rate calculations (FDR=0.2) using the Benjamini-Hochberg correction method to determine statistical significance (“TRUE” vs “FALSE”) when comparing raw cognitive test scores between participants with and without type 1 diabetes (main text, Table 2).

<i>i</i>	<i>p</i>	<i>q*</i>	<i>p < q*</i>	Factor
1	0.0000	0.0111	TRUE	DSST
2	0.0000	0.0222	TRUE	GP
3	0.0000	0.0333	TRUE	ROCF-copy
4	0.0005	0.0444	TRUE	NAART raw
5	0.0012	0.0556	TRUE	NAART scaled
6	0.0020	0.0667	TRUE	TMT Ratio B:A
7	0.0200	0.0778	TRUE	TMTB
8	0.0500	0.0889	TRUE	LN Sequence
9	0.0600	0.1000	TRUE	Stroop Color-Word
10	0.0960	0.1111	TRUE	FAS
11	0.1040	0.1222	TRUE	4WSTM, 5s list
12	0.1470	0.1333	FALSE	Animals
13	0.1700	0.1444	FALSE	4WSTM, 15s list
14	0.3400	0.1556	FALSE	RVLT interference
15	0.4100	0.1667	FALSE	ROCF-delay
16	0.4400	0.1778	FALSE	RVLT sum
17	0.6600	0.1889	FALSE	RVLT delay
18	0.7600	0.2000	FALSE	4WSTM, 30s list

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Supplementary Figure 1. Flow chart showing recruitment of participants with type 1 diabetes from the parent Pittsburgh Epidemiology of Diabetes Complications (EDC) Study into the ancillary neurocognitive/neuroimaging (MRI) study.



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Supplementary Figure 2. Standardized effect sizes of differences in raw cognitive test scores between participants with type 1 diabetes (Pittsburgh Epidemiology of Diabetes Complications Study) and without type 1 diabetes (Pittsburgh MR Hyper Study). Sample size for participants with type 1 diabetes provided above, numbers shown in parentheses (e.g., N=95). For participants without type 1 diabetes, N=138 for all tasks except NAART (NAART N=137).

